REMARKS

Upon entry of this amendment, claims 48, 49, 51-53, 55, 58 and 59 are presently pending. Claims 50, 54, 56 and 57 are canceled and claims 58 and 59 are added to claim specific anti-CEA and anti-idiotype antibodies that recognize CEA, which is disclosed in the specification. Any canceled subject matter is canceled without prejudice or disclaimer for filing in one or more continuing applications. The amendments to claims 48 and 52 are from the dependent claims that have been canceled. The inclusion of these features in these independent claims more clearly defines the present invention. Claims 58 and 59 are supported in the specification in Examples 1 and 2 on pages 30-32 and in Example 3 on pages 32-33. The inclusion of these latter claims does not raise any new issues that would require further search as Hansen is cited by the Examiner and reduces issues on appeal. Applicant respectfully requests entry of the amendment and consideration of the reply. Applicant acknowledges the Examiner's withdrawal of the double patenting rejection.

Rejection under 35 U.S.C. § 103(a)

Claims 48-57 remain rejected under 35 U.S.C. § 103(a) as obvious over Eshhar *et al.*, *Proc. Nat'l Acad. Sci. USA* **90:** 720 (1993), WO 92/15322, Wagner *et al.*, *Biotech. Therap.* **3:** 81 (1992), and "applicant's admission" at page 22 of the specification, in view of Hansen *et al.*, *Cancer* **71:** 3478 (1993) ("Hansen"). Applicant respectfully traverses this rejection.

The Examiner maintains her rejection of claims 48-57 for the same reasons as set forth in the previous Office Actions and thus maintains her position that Eshhar suggests the use of chimeric genes in adoptive immunotherapy. The Examiner maintains her position that Eshhar and Wagner show that such chimeric genes can be used in diseases caused by either tumors or infectious agent, and that this motivation comes from Eshhar. The Examiner takes the position that both the Eshhar 1993 and 1990 publications show that different research groups induce the cellular arm of the immune system.

The pending claims are directed to a method of inducing a cellular immune response against a tumor that expresses CEA by administering transfected T cells and then at least one cytokine. The present invention specifically achieves this response in one of two ways:

Firstly, (1) transfected T cells are administered in an effective immunostimulatory amount are produced by obtaining T cells from the patient and transfecting these T cells with an expression vector containing a DNA molecule encoding either a chimeric immunoglobulin/T cell receptor or a chimeric immunoglobulin/CD3 protein, and wherein the immunoglobulin-encoding portion of the DNA molecule encodes the variable region of an

antibody that binds with CEA or with an antigen associated with the infectious agent, and further wherein the variable regions of the α and β polypeptide chains of said T cell receptor are replaced by the variable regions of the antibody; and then (2) at least one cytokine is adminstered.

Secondly, (1) transfected T cells are administered in an effective immunostimulatory amount are produced by obtaining T cells from the patient and transfecting these T cells with an expression vector containing a DNA molecule encoding either a chimeric immunoglobulin/T cell receptor or a chimeric immunoglobulin/CD3 protein, and wherein the immunoglobulin-encoding portion of the DNA molecule encodes the variable region of an antibody that mimics an epitope of the CEA, and further wherein the variable regions of the α and β polypeptide chains of said T cell receptor are replaced by the variable regions of the antibody; and then (2) at least one cytokine is adminstered.

Neither Eshhar or Wagner disclose administering a cytokine after infusing the transfected T cells rather the Examiner appears to be arguing that Eshhar suggests that a cytokine, i.e., IL-2, is produced when the transfected T cells interact with the tumor. Applicant's specification on pages 25-30 discloses the preparation of the transfected T cells and the methods of using them to treat a patient. Particularly, page 30 lines 13-24 discloses methods to enhance the efficacy of adoptive immunotherapy. The administration of cytokines is performed after the administration of transformed T cells to amplify the immune response.

The Examiner's arguments are directed to combining Eshhar and Wagner to make the transfected T cells but as applicant noted above, the method requires the subsequent administration of at least one cytokine. Applicant submits that none of the prior art publications used in this obviousness rejection disclose administering a cytokine subsequent to the administration of the transfected T cells containing the DNA encoding the variable region of a Class III anti-CEA antbody or the DNA encoding the variable region of an anti-idiotypic antibody that recognizes a Class III anti-CEA antibody and nor do any of these publications provide a rationale for doing so. In view of these arguments and amendments to the claims, it is requested that this rejection of the pending claims be withdrawn.

CONCLUSION

Applicant kindly requests reconsider of the final rejection and entry of this amendment and response. The response does not raise any new issues and reduces issues on apply. The features added to independent claims 48 and 52 are present in the canceled dependent claims. In view of the foregoing, it is respectfully urged that the present claims are in condition for allowance. An early notice to this effect is earnestly solicited. Should there be any questions regarding this application, the Examiner is invited to contact the undersigned at the telephone number shown below.

Respectfully submitted,

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Date

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MARKED-UP COPY OF CLAIMS:

48. A method for inducing a cellular immune response in a patient against a tumor that expresses **carcinoembryonic antigen (CEA)** [a tumor associated antigen (TAA) or against a disease caused by an infectious agent], said method comprising:

administering an effective immunostimulatory amount of transfected T cells to a patient; and

subsequently administering at least one cytokine to said patient;

wherein said transfected T cells are produced by obtaining T cells from the patient and transfecting said T cells with an expression vector to obtain said transfected T cells;

wherein said expression vector comprises a DNA molecule encoding either a chimeric immunoglobulin/T cell receptor or a chimeric immunoglobulin/CD3 protein, and wherein said immunoglobulin-encoding portion of said DNA molecule encodes the variable region of [an antibody that binds with the TAA or with an antigen associated with the infectious agent] **a Class III anti-CEA antibody**, and further wherein the variable regions of the α and β polypeptide chains of said T cell receptor are replaced by said variable regions of the antibody.

52. A method for inducing a cellular immune response in a patient against a tumor that expresses **carcinoembryonic antigen (CEA)** [a tumor associated antigen (TAA) or against a disease caused by an infectious agent], said method comprising:

administering an effective immunostimulatory amount of transfected T cells to a patient; and

subsequently administering at least one cytokine to said patient;

wherein said T cells are produced by obtaining T cells from the patient and transfecting said T cells with an expression vector to obtain said transfected T cells;

wherein said expression vector comprises a DNA molecule encoding either a chimeric immunoglobulin/T cell receptor or a chimeric immunoglobulin/CD3 protein, and wherein said immunoglobulin-encoding portion of said DNA molecule encodes the variable region of an **anti-idiotypic antibody that recognizes a Class III anti-CEA antibody** [antibody that mimics an epitope of the TAA or an epitope of an antigen associated with the infectious agent], and further wherein the variable regions of the α

and β polypeptide chains of said T cell receptor are replaced by said variable regions of the antibody.